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Sporadic medullary thyroid carcinoma with a pedunculated intraluminal internal jugular vein recurrence: A case report and literature review

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ABSTRACT

Medullary thyroid carcinoma (MTC) is an uncommon usually slowly progressing neuroendocrine tumour that arises from calcitonin (CT) producing parafollicular C cells of the thyroid gland. It accounts for approximately 5% of all thyroid cancers. The majority of MTCs are sporadic (75%) whilst 25% are part of the MEN 2 hereditary syndrome (MEN 2A and MEN 2B and familial MTC). Mutations of the proto-oncogene, RET (Rearranged during Transfection), found on chromosome 10q11, are present in more than 95% of hereditary MTCs and about 25% of sporadic MTCs. MTC metastasizes primarily via lymphatic spread, to central, and lateral nodal neck compartments and the anterior and superior mediastinum. Distant haematogenous spread targets the lungs, liver, bone and brain, and is presumed to be secondary to a lymphatic pathway. There are no previously documented reports of a focal pedunculated metastases located within the jugular vein. We present the first reported case of a metastatic MTC lesion found in the right internal jugular vein in a man with recurrent MTC.

1. Introduction

Medullary thyroid carcinoma (MTC) is an uncommon usually slowly progressing neuroendocrine tumour that arises from calcitonin (CT) producing parafollicular C cells of the thyroid gland.[1–4] It accounts for approximately 5% of all thyroid cancers.[5,6] The majority of MTCs are sporadic (75%) whilst 25% are part of the MEN 2 hereditary syndrome (MEN 2A and MEN 2B and familial MTC).[7,8] Mutations of the proto-oncogene, RET (Rearranged during Transfection), found on chromosome 10q11, are present in more than 95% of hereditary MTCs and about 25% of sporadic MTCs.[9] MTC metastasizes primarily via lymphatic spread, to central, and lateral nodal neck compartments and the anterior and superior mediastinum. Distant haematogenous spread targets the lungs, liver, bone and brain, and is presumed to be secondary to a lymphatic pathway. There are no previously documented reports of a focal pedunculated metastases located within the jugular vein. We present the first reported case of a metastatic MTC lesion found in the right internal jugular vein in a man with recurrent MTC.

2. Case

A 54 year old man presented to his local hospital in February 2008 with a right sided thyroid mass. An ultrasound scan and fine needle aspiration cytology (FNAC) were inconclusive. In March 2008 he underwent a diagnostic right thyroid lobectomy from which he made a good recovery. Histological analysis of this specimen revealed a 2 cm MTC. The patient was referred to Hammersmith Hospital for further care.

The post-operative calcitonin and carcinoembryonic antigen (CEA) levels were 35 ng/L (normal range <11.8 ng/L) and 7 ug/L (normal range 0–5 ug/L), respectively. An ultrasound scan (USS) of the neck did not reveal lymphadenopathy. Following normal urinary catecholamine and metanephrine estimation and a negative genetic screen for MEN2 syndrome the patient proceeded to a completion thyroidectomy with bilateral prophylactic neck dissection in April 2008. There was no evidence of medullary carcinoma in the remnant left thyroid lobe and none of the 45 central or left lateral cervical lymph nodes removed contained malignant deposits. However 4 of the 43 lymph nodes removed from the right central and right lateral neck were positive for medullary carcinoma (1 lymph node from the right central compartment and 3 cervical nodes from levels 2–4). The patient made a good recovery with a normal serum calcium on no supplements at 2 week follow up. After an initial fall in the calcitonin and CEA levels (to 13.4 ng/L and 2 ug/L respectively) in the subsequent months the calcitonin levels began to rise to pre-re-operative surgery levels suggesting low grade persistent disease (Figs. 1 and 2). A magnetic resonance (MRI) scan and USS of the neck were performed in May 2009 revealing only cytologically proven small reactive lymph nodes.

A (whole body) pentavalent dimercaptosuccinic acid (DMSA) scan was performed (July 2009) which showed no evidence of disease. By January 2010, the calcitonin and CEA levels had risen to136 ng/L and a fluoro-deoxy-D-glucose – positron emission

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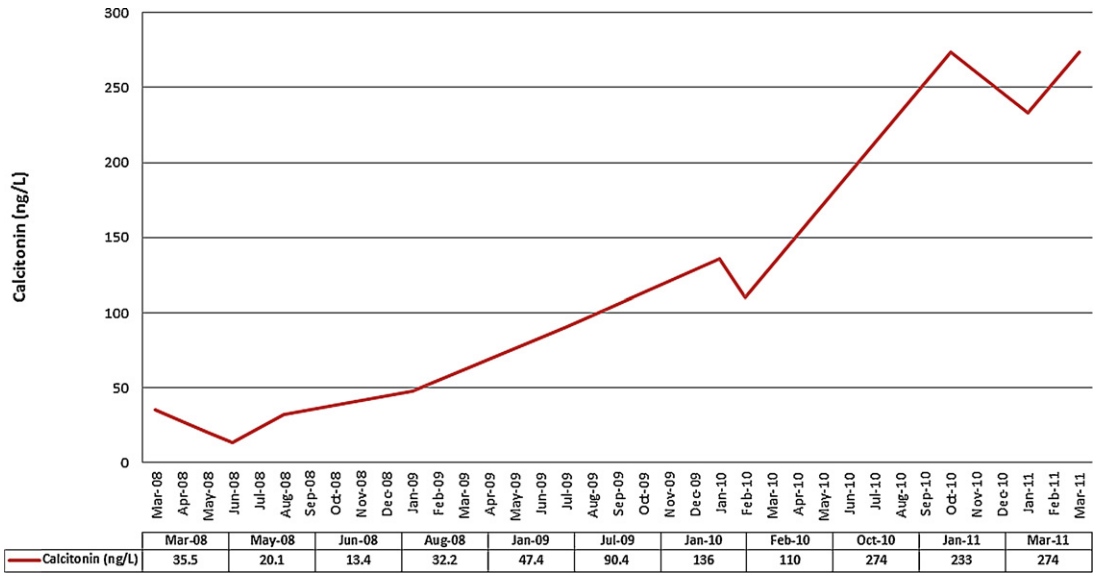
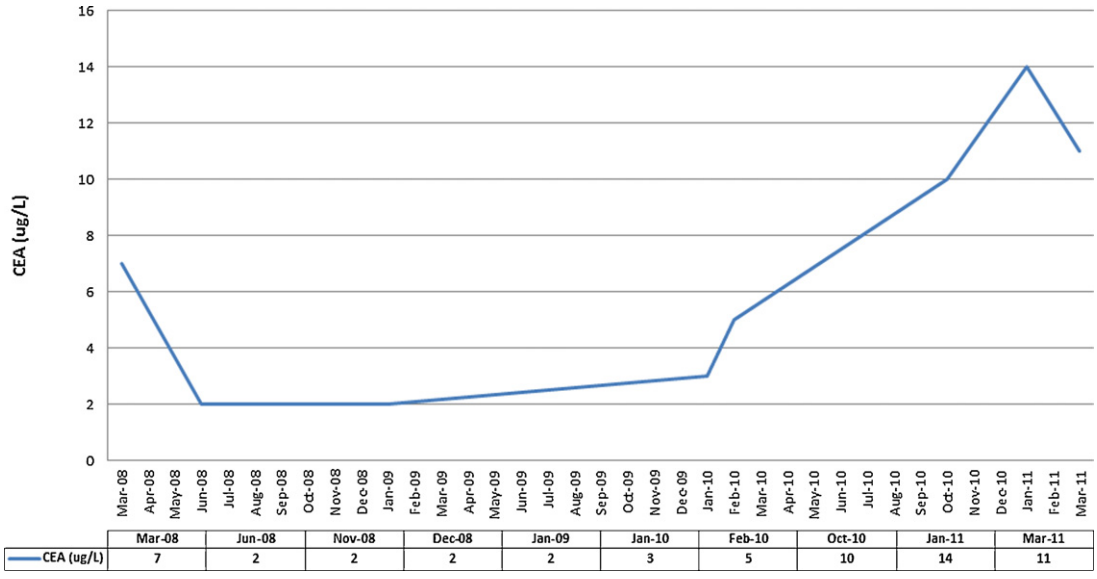


	Mar-08	May-08	Jun-08	Aug-08	Jan-09	Jul-09	Jan-10	Feb-10	Oct-10	Jan-11	Mar-11
Calcitonin (ng/L)	35.5	20.1	13.4	32.2	47.4	90.4	136	110	274	233	274

Fig. 1. Graph showing serum calcitonin levels from March 2008 to March 2011.



	Mar-08	Jun-08	Nov-08	Dec-08	Jan-09	Jan-10	Feb-10	Oct-10	Jan-11	Mar-11
CEA (ug/L)	7	2	2	2	2	3	5	10	14	11

Fig. 2. Graph showing serum CEA levels from March 2008 to March 2011.

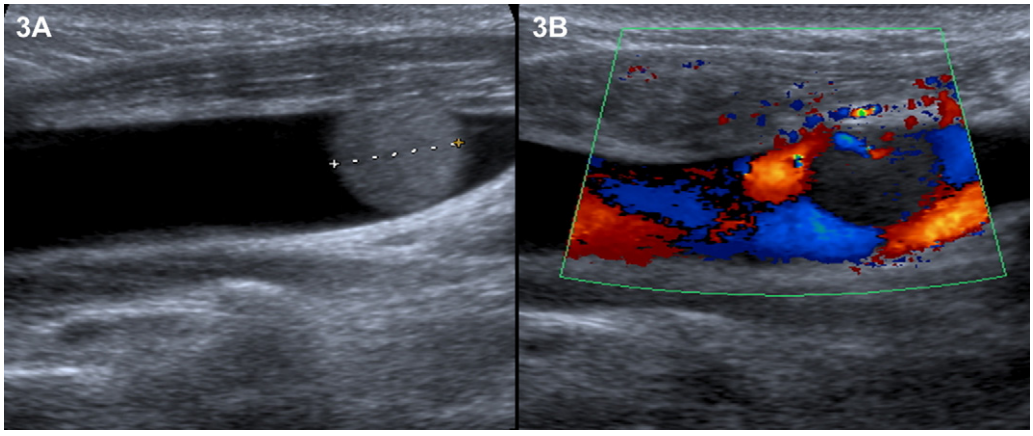


Fig. 3. (A) Ultrasound image of the 10 mm pedicled spherical lesion within the RIJV. (B) Ultrasound image showing pedicled lesion obtaining blood supply from adjacent tissues.

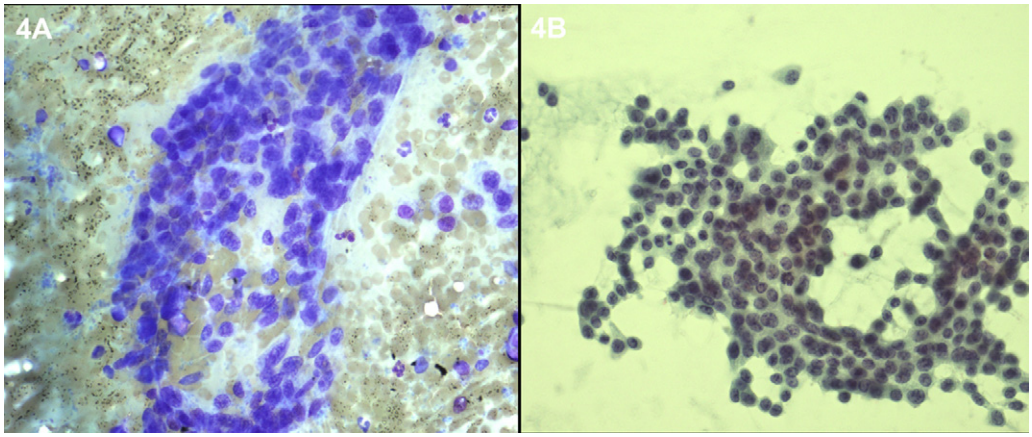


Fig. 4. (A and B) Microscopic images of the FNAC (performed on the neck nodes) stained with May Grunwald Giemsa (A) and Papanicolaou (B), showing tumour composed of cohesive islands of cells with neuroendocrine features including granular ('salt and pepper') chromatin (×20).

Fig. 5. (A and B) Macroscopic images (A) showing internal aspect of the sacrificed right IJV with a 10 mm polypoid lesion situated to the right. (B) Magnified view.

tomography (FDG-PET) scan of the entire body, performed in February 2010, revealed no evidence of metabolically active disease. The patient remained asymptomatic but by October 2010, the calcitonin and CEA levels had risen to 274 ng/L and 10 ug/L, respectively. At this time examination of the neck revealed a fullness at level 2 on the right. An USS of the neck revealed a 10 mm well-defined pedunculated mass laying within the right internal jugular vein (RIJV) and possessing an independent blood supply (Fig. 3A and B).

Reactive looking lymph nodes were also visualised on the right side of the neck at level 3. One of the nodes underwent FNAC which revealed dispersed nests of intermediate sized epithelial-like cells with granular chromatin and occasional nucleolus with dense moderately abundant cytoplasm (Fig. 4A and B). Immunocytochemistry on the thinprep sample revealed expression of calcitonin and nuclear expression of TTF-1 in keeping with metastatic medullary carcinoma.

In view of these findings the patient underwent a repeat uncomplicated right selective neck dissection (levels 2–4) with sacrifice of the right IJV in February 2011 (Fig. 5A and B and Fig. 6). He made a good recovery and was discharged 3 days following surgery.

Histological analysis confirmed a 10 mm × 10 mm × 10 mm polypoid lesion, showing features consistent with metastatic medullary carcinoma of the thyroid, and with a stalk measuring 0.3 cm in length. The tumour reached the endothelial surface of the vein (Fig. 7A and B). Resection margins of the vein were free of tumour. In addition, metastatic medullary carcinoma was found in just 1 of the 19 dissected lymph nodes.

The patient attended clinic in March 2011 and remains asymptomatic, with normal haemoglobin, calcium, urea and creatinine levels. However the calcitonin and CEA levels remain significantly raised at 274 ng/L and 11 ug/L, respectively and have further increased to 437 ng/L and 13 ug/L, respectively in May 2011 in keeping with as yet unidentified distant metastasis.

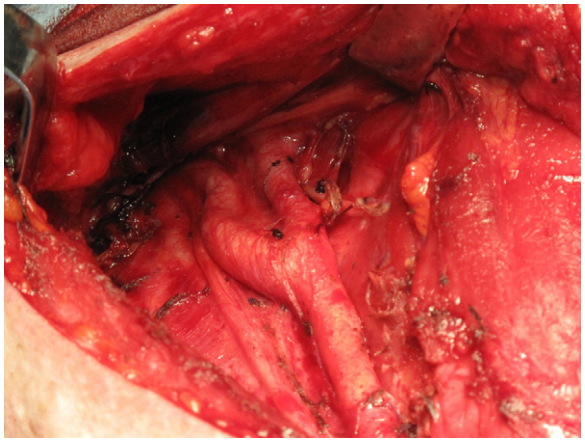


Fig. 6. Right side of neck post excision of RIJV and lymph node dissection (levels 2–4) demonstrating right common carotid artery and its bifurcation and right vagus nerve.

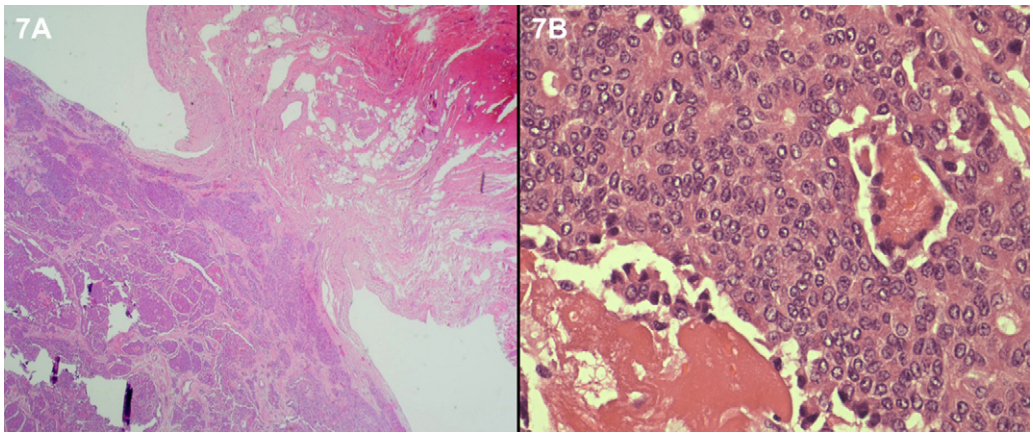


Fig. 7. (A and B) H&E stained histological images showing the pedunculated metastatic deposit (lower left) attached to the vessel wall (A) ((×2) and a high power view (B) showing uniform polygonal tumour cells arranged in sheets and rosettes (indicative of neuroendocrine differentiation) consistent with medullary carcinoma. Amyloid is also present between tumour islands ((×20).

3. Discussion

Patients with sporadic MTC typically present with a solitary, palpable thyroid nodule or cervical lymphadenopathy.[10] Less commonly the presentation is with local compressive or invasive symptoms such as hoarseness, dysphagia or diarrhoea secondary to high levels of circulating calcitonin.[7] Lymph node metastasis is present in 50% of patients presenting with a palpable thyroid mass/nodule.[11] The central (level 6) followed by the lateral compartments (levels 2–5) are the most common sites of lymph node metastases. Further spread can occur to the contralateral cervical lymph nodes and then to the mediastinal (level 7) nodes.[11,12] Distant MTC metastases usually occur via haematogenous spread to the lungs, liver, bone and brain with the consequent potential symptoms of abdominal discomfort, bone pain or change in cognitive state.[11,12]

A timely diagnosis of MTC is achieved via a thorough history, including a comprehensive family history with direct questioning regarding associated diseases in familial disease, and a complete examination of the neck. FNAC, ideally with immunohistochemical staining for calcitonin aids diagnosis but may not always be diagnostic.[7,8] In addition the routine or targeted measurements of serum calcitonin may be adopted to screen or confirm a suspicion of MTC when suspected.[7,8] Genetic analysis for RET mutations, and screening for phaeochromocytoma with measurements of plasma or urinary metanephrines and catecholamines as well as vocal cord analysis are mandatory.[13] For patients with elevated calcitonin levels, USS for the assessment of lymphadenopathy is recommended alone or with computer tomography (CT) or magnetic resonance imaging (MRI) of the chest and mediastinum.[13]

The mainstay of treatment of MTC is surgical resection since MTC do not capture and concentrate iodine and at present show poor response to available adjuvant regimens in all but advanced disease. For this reason a pre-operative diagnosis and optimal first time surgery represent key to good patient outcomes to the point that the first operation in MTC remains a key predictor of outcome. The American Thyroid Association (ATA) and National Comprehensive Cancer Network (NCCN) have released guidelines on management of MTC depending on size of the resected tumour.[13,14] For unilateral tumours less than 1 cm a total thyroidectomy is recommended with the consideration of dissection of the level 6 lymph nodes. For MTC tumours greater than or equal to 1 cm and/or multifocal disease, total thyroidectomy with routine bilateral central neck dissection is advocated. For ipsilateral or contralateral cervical lymph nodes that are clinically or radiologically apparent, ipsilateral or bilateral modified neck dissection, respectively, are advocated.[13]

The patient reported above underwent a diagnostic right thyroid lobectomy due to an inconclusive USS and FNAC. Despite subsequent radical surgery the disease remained poorly controlled. The unusually sited and relatively large metastasis within the IJV was eventually detected with neck USS but not detected with DMSA or FDG PET-CT scans. Tumour thrombi in the IJV from FTC and PTC are well documented but no reports of MTC thrombi have been documented in a recent review of tumour thrombi.[15] However it is clear that the implications of such findings – a very high risk of distant metastasis – remain true to MTC as well as PTC.

The postoperative management and surveillance of MTC is based on regular serum calcitonin measurements and targeted imaging.[16] Serum CEA levels may be normal in patients with preclinical MTC but may be useful during follow-up because high concentrations or rapidly increasing concentrations indicate disease progression or dedifferentiation.[17] If a significant rise in calcitonin or CEA occurs following thyroidectomy, further imaging investigations (USS neck, CT, MRI, FDG-PET or bone scan) are recommended to look for locally recurrent or metastatic disease.[16] For asymptomatic patients with negative imaging, surveillance 6-monthly calcitonin and CEA is recommended.[7,16]

The strongest predictors of prognosis in patients with MTC are stage of the disease and the extent of surgery.[6,8,18,19] Patients under the age of 65 (at time of diagnosis), who undergo surgery, and who have a total thyroidectomy as opposed to a lobectomy, have been shown to have longer survival. Improved outcome is associated with female gender, well-diffferentiated histology, small tumour size confined to the capsule of the thyroid, lack of lymph node involvement, and low post-thyroidectomy calcitonin levels.[6,18,20,21] The overall 5- and 10-year survival rates for MTC have been reported to be between 80–97% and 75–88% respectively of which the higher numbers having been obtained from more recent reviews.[19,21]

4. Conclusion

This is the first English language report of a pedunculated tumour thrombus from MTC located in the internal jugular vein. The importance of appropriate first time surgery in MTC cannot be over-emphasised. The difficulty in the localisation recurrent or persistent distant spread of MTC remains a major challenge.

Conflicts of interest statement

None.

Funding

None.

Consent

Consent from the patient in question has been sought and is readily available upon request.

Author contributions

Dr. Darren K. Patten – contributed to writing of the article and acquisition of pictures and construction of figures. Dr. Rashpal Flora – provided us with the histological pictures and corresponding microscopic descriptions. Mr. Neil Tolley – contributed to the reading and correction of the manuscript. Mr. Fausto Palazzo – conception of project and review/correction of article before submission.

References

1. Chi DD, Moley JF. Medullary thyroid carcinoma: genetic advances, treatment recommendations, and the approach to the patient with persistent hypercalcitoninemia. *Surg Oncol Clin N Am* 1998;**October (7)**(4):681–706. Review.
2. Kaserer K, Scheuba C, Neuhold N, Weinhäusel A, Haas OA, Vierhapper H, et al. Sporadic versus familial medullary thyroid microcarcinoma: a histopathologic study of 50 consecutive patients. *Am J Surg Pathol* 2001;**25**(October(10)):1245–51.
3. Kaserer K, Scheuba C, Neuhold N, Weinhäusel A, Vierhapper H, Haas OA, et al. C-cell hyperplasia and medullary thyroid carcinoma in patients routinely screened for serum calcitonin. *Am J Surg Pathol* 1998;**22**(June(6)):722–8.
4. Weinhaeusel A, Scheuba C, Lauss M, Kriegner A, Kaserer K, Vierlinger K, et al. The influence of gender, age, and RET polymorphisms on C-cell hyperplasia and medullary thyroid carcinoma. *Thyroid* 2008;**18**(December(12)):1269–76.
5. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973–2002. *JAMA* 2006;**295**(May 10(18)):2164–7.
6. Kebebew E, Ituarte PH, Siperstein AE, Duh QY, Clark OH. Medullary thyroid carcinoma: clinical characteristics, treatment, prognostic factors, and a comparison of staging systems. *Cancer* 2000;**88**(March 1(15)):1139–48.
7. Fialkowski EA, Moley JF. Current approaches to medullary thyroid carcinoma, sporadic and familial. *J Surg Oncol* 2006;**94**(December(158)):737–47. Review.
8. Moo-Young TA, Traugott AL, Moley JF. Sporadic and familial medullary thyroid carcinoma: state of the art. *Surg Clin North Am* 2009;**89**(October(5)):1193–204. Review.
9. Liu Z, Falola J, Zhu X, Gu Y, Kim LT, Sarosi GA, et al. Antiproliferative effects of Src inhibition on medullary thyroid cancer. *J Clin Endocrinol Metab* 2004;**89**(July(7)):3503–9.
10. Moley JF, Shervin N. Medullary carcinoma. In: Clark O, Duh Q-Y, Kebebew E, editors. *Textbook of endocrine surgery*. 2nd ed. Philadelphia: Elsevier Saunders; 2005. pp. 129–41.
11. Moley JF, DeBenedetti MK. Patterns of nodal metastases in palpable medullary thyroid carcinoma: recommendations for extent of node dissection. *Ann Surg* 1999;**229**(June(6)):880–7, discussion 887–8.
12. Musholt TJ, Goodfellow PJ, Scheumann GF, Pichlmayr R, Wells Jr SA, Moley JF. Differential display in primary and metastatic medullary thyroid carcinoma. *J Surg Res* 1997;**69**(April(1)):94–100.
13. Tuttle RM, Ball DW, Byrd D, Daniels GH, Dilawari RA, Doherty GM, et al. National comprehensive cancer network. medullary carcinoma. *J Natl Compr Canc Netw* 2010;**8**(May(5)):512–30.
14. American Thyroid Association Guidelines Task ForceKloos RT, Eng C, Evans DB, Francis GL, Gagel RF, et al. Medullary thyroid cancer: management guidelines of the American Thyroid Association. *Thyroid* 2009;**19**(June(6)):565–612. Review. Erratum in: Thyroid. 2009 Nov;19(11):1295.
15. Kobayashi K, Hirokawa M, Yabuta T, Fukushima M, Kihara M, Higashiyama T, et al. Tumor thrombus of thyroid malignancies in veins: importance of detection by ultrasonography. *Thyroid* 2011;**21**(May(5)):527–31.
16. Pitt SC, Moley JF. Medullary, anaplastic, and metastatic cancers of the thyroid. *Semin Oncol* 2010;**37**(December(6)):567–79. Review.
17. Pacini F, Castagna MG, Cipri C, Schlumberger M. Medullary thyroid carcinoma. *Clin Oncol (R Coll Radiol)* 2010;**22**(August(6)):475–85. Review.
18. Gilliland FD, Hunt WC, Morris DM, Key CR. Prognostic factors for thyroid carcinoma. A population-based study of 15,698 cases from the Surveillance, Epidemiology and End Results (SEER) program 1973–1991. *Cancer* 1997;**79**(February 1(3)):564–73.
19. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National cancer data base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985–1995. *Cancer* 1998;**83**(December 15(12)):2638–48.
20. Roman S, Lin R, Sosa JA. Prognosis of medullary thyroid carcinoma: demographic, clinical, and pathologic predictors of survival in 1252 cases. *Cancer* 2006;**107**(November 1(9)):2134–42.
21. Clark JR, Fridman TR, Odell MJ, Brierley J, Walfish PG, Freeman JL. Prognostic variables and calcitonin in medullary thyroid cancer. *Laryngoscope* 2005;**115**(August(8)):1445–50.